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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/978,633	11/25/1997	ELAZAR RABBANI	Enz-53(D1)	4639

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
05/11/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/978,633	RABBANI ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *245-248,251,253,261-265,306 and 307* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *245-248,251,253,261-265,306 and 307* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for this application is now Kimberly Chong whose contact information is provided below.

Status of Application/Amendment/Claims

Applicant's response filed 02/17/2011 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 08/17/2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 02/17/2011, claims 245-248, 251, 253, 261-265, 306 and 307 are pending in the instant application.

Maintained Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 275, 289, 290, 296-301 of copending Application No. 08/978,634 for the reasons of record set forth in the Office action mailed 11-23-09. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods and cell delivery compositions comprising covalently bound polynucleotides, targeting ligands and polypeptides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No arguments have been made concerning this rejection.

Claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-5 of copending Application No. 11/929,897 for the reasons of record set forth in the Office action mailed 11-23-09. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims

are drawn to cell delivery compositions comprising covalently bound polynucleotides, targeting ligands and optionally further comprising polypeptides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No arguments have been made concerning this rejection.

Claim Rejections - 35 USC § 112

The rejection of claims 245-248, 251, 253, 261-265, 306 and 307 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons of record.

Applicant's arguments filed 02/17/2011 have been fully considered but they are not persuasive. Applicant argues the specification provides an extensive disclosure of each aspect of the claimed method and this along with the state of the art in molecular biology being very predictable would provide to an adequate description of the claimed invention. This argument is not convincing because simply describing specific components of the construct and methods is not sufficient to adequately describe the distinguishing features or attributes concisely shared by the members of the expansive genus of nucleic acid constructs.

Applicants submit that the answers poised by the Office action would be understood based on the state of the art or could be achieved with only routine experimentation. This is not persuasive because the claimed genus reads on a broad

array of structures and the disclosure fails to provide a representative number of species for such a broad genus that would provide the claimed function of cell delivery to any cell in an organism in vivo or in vitro. Applicants recite examples of relevant state of the art wherein the non-nucleic acid component directs the nucleic acid component for targeted gene expression.

The reference cited, while describing DNA complexes that can target specific cells for targeted gene expression, do not provide any guidance to lead one of skill in the art to a particular species from the broad genus claimed such that this species would have the required function as claimed. Nothing in the recited references describe the distinguishing characteristics or features of the claimed structure in such a way as to convey that the inventor had possession of the claimed genus.

Describing each element and the routine nature of the art as argued by Applicant would not lead the skilled artisan to conclude that Applicants had possession of the claimed construct and methods. For example, the skilled artisan would not know how big the first nucleic acid strand would need to be such that a second nucleic acid strand is fully complementary and is capable of forming a double stranded structure that is a template for synthesis of any nucleic acid product. This description as well as questions poised in the previous Office action could not be achieved with only routine experimentation.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to concretely describe the broad genus claimed, and which provide for the functions claimed, of being successfully transformed

into a desired target cell in an organism, and of successfully expressing recombinant constructs in a target cell in vitro or in vivo).

Thus, Applicant was not in possession of the expansive genus of constructs claimed.

The rejection of claims 245-248, 251, 253, 261-265, 306 and 307 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record. Applicant's arguments filed 02/17/2011 have been fully considered but they are not persuasive.

Applicant argues five of the references cited in the Office action only discuss the predictability of antisense therapeutics and the claims are not so limited. In response, because of the breadth of the nucleic acid product synthesized from the claimed structure and because this breadth encompasses antisense oligonucleotides, this oligonucleotide was discussed as one aspect of the lack of enablement.

Applicant argues the instant claims with the exception of claims 263-265 and 307 are drawn to composition claims and not methods and the Office action does not provide any indication that the compositions are not enabled.

The lack of enablement rejection was based on the specification and claims not enabling any person skilled in the art to *make* and use the claimed invention. The claims are drawn to nucleic acid constructs and compositions comprising non-natural structures which comprising a double-stranded portion that synthesizes a nucleic acid product when administered to cells. The claims require the constructs be assembled,

transfected into target cells in vitro or in vivo, and produce and express the recombinant products encoded therein. The instant application does not provide an enabling disclosure such that the skilled artisan would be capable of making a nucleic acid construct from the broadly claimed elements such that the construct upon introduction into any cell type would be capable of synthesizing a nucleic acid product.

The previously cited art summarizes the state of the art with respect to delivery of a nucleic acid such that synthesis/expression of a nucleic acid product in the cell, such as antisense, siRNA or ribozymes, and the unpredictability of such delivery. Since the specification fails to provide any particular guidance or concrete examples for the successful targeting or delivery of a representative number of species of the broad genus of compounds claimed, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention using the broad array of constructs claimed.

The disclosure teaches schematics of nucleic acid constructs comprising multiple nucleic acid components (3 and 4 segment components) and domains for target cell binding (see figures 4, 6, 15-8) and for recombinant expression in a target cell. But no reduction to practice has been provided for the instant schematics, whereby the proposed structures are successfully targeted to and transfected into target cells, remain intact as schematically depicted, and produce the recombinant nucleic acids or protein expression products in a predictable manner.

Applicants have not provided guidance in the specification toward a method of delivery of a representative number of species, or any concrete examples in vitro or in

vivo. Applicants have not provided adequate written description for the compositions claimed, nor the successful use of any representative number of species of the broadly claimed genus whereby any concrete examples of intact delivery and recombinant expression are provided.

The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of the specific nucleic acid sequences and components necessary to make the nucleic acid constructs and compositions to target any cell type, determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues, whereby a representative number of the nucleic acid structures representing this diverse and expansive genus claimed are successfully delivered to the target cells or tissues in vitro or in vivo intact, and further whereby recombinant expression is provided from the intact constructs in vitro and in the intended target cells in a subject.

Thus the specification does not reasonably provide enablement for making and using a representative number of species of the genus of constructs claimed, wherein the constructs are assembled, transfected into target cells in vitro or in vivo, and produce and express the recombinant products encoded therein and for these reasons, it would require undue experimentation beyond that provided in the instant specification to make and use the array of constructs as instantly claimed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact the SPE for 1635 Heather Calamita at 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
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Art Unit 1635